23

- (b) contacting an aqueous solution of plasmid with said mixture prepared in step (a) to provide a single phase; and
- (c) removing said organic solvent to provide a suspension of plasmid-lipid particles, wherein said plasmid is 5 encapsulated in a lipid layer and said particles are resistant to degradation in serum, and wherein the particles have a diameter ranging from about 50 to about 150 nm.
- **15**. A method in accordance with claim **10**, wherein said <sup>10</sup> non-cationic lipids comprise a polyethylene glycol-lipid conjugate.
- **16**. A method in accordance with claim **15**, wherein said polyethylene glycol-lipid conjugate is a PEG-ceramide conjugate.
- 17. A method in accordance with claim 14 further comprising;
  - (d) sizing said plasmid-lipid particles to achieve a uniform particle size.
- 18. A method in accordance with claim 10, wherein said <sup>20</sup> cationic lipids are selected from the group consisting of DODAC, DDAB, DOTAP, DOTMA, DOSPA, DOGS, DC-Chol and combinations thereof.
- **19**. A method in accordance with claim **14**, wherein said non-cationic lipids are selected from the group consisting of DOPE, POPC, EPC and combinations thereof.
- 20. A method for introducing a plasmid into a cell, comprising:
  - (a) preparing a plasmid-lipid particle according to the method of claim 14; and
  - (b) contacting said cell with said plasmid-lipid particle for a period of time sufficient to introduce said plasmid into said cell.
- 21. A method in accordance with claim 20, wherein said plasmid-lipid particle comprises a plasmid, DODAC, POPC and a PEG-Ceramide selected from the group consisting of PEG-Cer- $\rm C_{20}$  and PEG-Cer- $\rm C_{14}$ .
- **22.** A method in accordance with claim **20,** wherein said plasmid-lipid particle comprises a plasmid, DODAC, DOPE and a PEG-Ceramide selected from the group consisting of PEG-Cer- $\rm C_{20}$  and PEG-Cer- $\rm C_{14}$ .
- 23. In a method of gene therapy involving the introduction of a plasmid via a plasmid-lipid composition into a cell resulting in sufficient expression to effect a phenotypic 45 change, the improvement which comprises
  - (a) preparing a plasmid-lipid particle according to the method of claim 14; and
  - (b) contacting said cell with said plasmid-lipid particle for a period of time sufficient to introduce said plasmid into 50 said cell.

24

- **24**. A method for the preparation of serum-stable plasmid-lipid particles, comprising:
  - a) combining a plasmid with cationic lipids in a first detergent solution to provide a coated plasmid-lipid complex;
  - b) contacting non-cationic lipids with said coated plasmid-lipid complex to provide a second solution comprising detergent, a plasmid-lipid complex and non-cationic lipids and adding a polyethylene glycollipid conjugate to said second solution; and
  - c) removing said detergent from said second solution to provide a solution of serum-stable plasmid-lipid particles, wherein said plasmid is encapsulated in a lipid bilayer and said particles are resistant to degradation in serum, and wherein the particles have a diameter ranging from about 50 to about 150 nm.
- **25**. A method for the preparation of serum-stable plasmid-lipid particles, comprising:
  - a) preparing a mixture comprising cationic lipids and non-cationic lipids in an organic solvent, wherein said non-cationic lipids comprise a polyethylene glycollipid conjugate;
  - b) contacting an aqueous solution of plasmid with said mixture prepared in step (a) to provide a single phase;
  - c) removing said organic solvent to provide a suspension of plasmid-lipid particles, wherein said plasmid is encapsulated in a lipid bilayer and said particles are resistant to degradation in serum, and wherein the particles have a diameter ranging from about 50 to about 150 nm.
- **26**. A method in accordance with claim **25**, wherein said polyethylene glycol-lipid conjugate is a PEG-ceramide conjugate.
- 27. A method for introducing a plasmid into a cell, comprising:
  - (a) preparing a plasmid-lipid particle according to the method of claim 25; and
  - (b) contacting said cell with said plasmid-lipid particle for a period of time sufficient to introduce said plasmid into said cell
- **28**. A method in accordance with claim **27**, wherein said plasmid-lipid particle comprises a plasmid, DODAC, POPC and a PEG-Ceramide selected from the group consisting of PEG-Cer-C<sub>20</sub> and PEG-Cer-<sub>14</sub>.
- **29**. A method in accordance with claim **27**, wherein said plasmid-lipid particle comprises a plasmid, DODAC, DOPE and a PEG-Ceramide selected from the group consisting of PEG-Cer-C<sub>20</sub> and PEG-Cer-C<sub>14</sub>.

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